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Assessment of thyroid functions in patients with opioid use disorder

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Abstract

Aim: In recent years, there has been an increase in substance use prevalence. Endocrine and metabolic changes are known in substance use disorders. There are limited studies evaluating opioid effects on thyroid hormones. Studies about effects of addictive substances on the body indicate that opioid use affects thyroid functions via the hypothalamic-hypophyseal axis. In this study, we aimed to compare the thyroid dysfunctions of patients with opioid substance use disorder and those with non-opioid substance use disorder. Material and Method: The study group consisted of 175 inpatients with substance use disorders defined by the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) criteria between 2015 and 2017. Serum TSH, fT4, fT3 levels of admitted patients were retrospectively screened. The patients were divided into three groups as opioid, non-opioid, and multiple substance users. Serum TSH, fT4, fT3 levels were compared between three groups. Results: Patients with only opioid use disorder had significantly lower serum TSH levels than those with non-opioid use disorder (p=0.018). TSH levels were significantly lower in patients with multiple substance users (opioid and non-opioid) compared with the patients with non-opioid subjects (p=0.006). However, there were no statistically significant differences between the groups in terms of fT3 and fT4 levels (p=0.756, p=0.467). Discussion: Opioid substance causes many physiological changes in the body. Endocrine reflections have been different depending on the type of substance used. This study suggests that opioid substance may also affect thyroid functions. Therefore, thyroid functions must be evaluated in patients with opioid use disorders.

Keywords

TSH, Thyroid Hormones; Substance Use Disorder; Opioid; Tetrahydrocannabinol

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Introduction

The prevalence of substance use has increased in recent years. Cannabis has been identified as the most widely used illicit drug in the general population in Turkey and in the World. Among the participants, 0.7% reported that they used cannabis at least once in their lifetime in Turkey [1]. In the study conducted by Çakmak and Evren in 2006, the number of patients admitted to the Center for Treatment and Research of Alcohol and Substance Abuse has been shown to increase since the past [2]. In a study conducted in university students in 2017, 3184 people were included in this study, and 1020 students reported using substance abuse at least once and 225 reported having a history of substance abuse at least five times [3].

Due to the large spectrum of addictive substances, their effects on organisms are still being investigated. In addition to behavioral and cognitive discrepancies, opiate dependence also reveals physiological symptoms [4]. It has been shown that opiate use decreases adinopectin levels and increases the risk of development of metabolic disorders [5]. Apart from psychiatric symptoms such as coronary artery disease, diabetes mellitus can cause metabolic diseases [5,6].

Most opioid are mu receptor agonists and effect receptors in the central nervous system. These effects disturb the hormonal balance of the hypothalamic-pituitary as in other neural tissues [7]. Different results have been obtained in this axle especially in terms of its effects on thyroid hormones. In a study on rats, there was a decrease in TSH levels after morphine injection and no difference in T3 and T4 levels [9]. In a controlled study, increase in total T3 levels and changes in TSH levels were observed [8]. The aim of this study was to compare the thyroid function tests of patients according to the type of substance used by the patients diagnosed with substance use disorder.

Material and Method

Patients diagnosed with substance use disorder according to the DSM–5 criteria and treated in the psychiatry clinic between January 2015 and December 2017 were included in this retrospective study. Patients were detected in this review of inpatients records. Patients with hypothyroidism, hyperthyroidism, and history of thyroid surgery were excluded from the study. Firstly, 160 cases were included in this study; patients are divided into three groups: opiate, non-opiate, and multiple substances (opiate and non-opiate) use disorders.

The number of patients using non-opiate substance was determined as 15, and the first 15 persons with non-opiate substance use were included in the study by retrospective screening before January 2015 for statistical comparison. A total of 175 people were included in the study. Thyroid hormone concentrations were measured using the electrochemiluminescence immunoassey method. TSH, free T4, free T3 hormone levels, and categorical and numerical variables were compared between the groups. The approval for the study was obtained from the Ethics Committee before the collection of data.

Data analysis was performed on SPSS Windows 22.0 software. Percentage, arithmetic mean, and standard deviation values were used. The normal distribution of numerical variables was tested with the Shapiro- Wilk test. ANOVA and LSD tests were used for comparison of normally distributed numerical variables in three groups; the Kruskall-Wallis and All Pairwise tests were used to compare the numerical variables that do not distribute normally. The relationships between categorical variables were tested with the Chi-Square test.

Results

One hundred and seventy-five cases were included in the study with the diagnosis of substance use disorder. Thirty-five (20%) of the cases were diagnosed as opiate use disorder, 30 (17%) were non-opiate substance use disorder and 110 (62%) were diagnosed as multiple substance use disorder. There were no significant differences between the groups in terms of age, sex, duration of hospitalization, psychiatric comorbidities, use of the intravenous substance, the presence of forensic events, and history of treatment due to substance use disorder. There were significant differences between the groups in terms of age of onset of substance use, duration of substance use, self-mutilating behaviors, the presence of psychotic features (p=0.048, p=0.016, p=0.013, p=0.004) (Table 1 and Table 2). When hormone levels indicating thyroid function were examined, a significant difference was found in TSH levels between the groups; there was no statistically significant difference between the groups for free T3 and free T4 levels (Table 3). In binary comparison, TSH levels were significantly higher in patients with non-opiate use than those in opiate patients (p = 0.002) and multiple substance use (p = 0.014).

Table 1. Sociodemographic data

		Substance type						
		Opiate		Non Opiate		Multiple substance		
		Sayı	%	Sayı	%	Sayı	%	P
sex	Male	34	97,1%	30	100,0%	102	92,7%	0,239
	Female	1	2,9%	0	0,0%	8	7,3%	
Comorbidities	No	25	71,4%	15	50%	70	63,6%	0,460
	Yes	10	28,6%	15	50%	40	36,4%	
IV use	No	27	77,1%	30	100,0%	91	82,7%	0,139
	Yes	8	22,9%	0	0,0%	19	17,3%	
Self mutilation	No	22	62,9%	20	66,7%	43	39,1%	0,013*
	Yes	13	37,1%	10	33,3%	67	60,9%	
Forensic History	No	27	77,1%	22	73,3%	74	67,3%	0,517
	Yes	8	22,9%	8	26,7%	36	32,7%	
Substance use disorder treatment	No	19	54,3%	16	57,1%	43	39,1%	0,169
	Yes	16	45,7%	12	42,9%	67	60,9%	
Psychotic features	No	34	97,1%	22	78,6%	77	70,0%	0,004*
	Yes	1	2,9%	8	21,4%	33	30,0%	

Table 2. Numerical variable according to substance type

	Age			Duration of hospitalization		Onset age		Duration of substance use	
	N	Mean± Std. Deviation	P	Mean± Std. Deviation	P	Mean± Std. Deviation	P	Mean± Std. Deviation	P
Opiate	35	27,68±9,05	0,522	9,51±2,58	0,666	21,94±9,17	0,048*	5,17±4,65	0,016*
Non Opiate	30	26,34±7,12		9,43±5,71		22,95±7,01		5,34±4,46	
Multiple	110	26,14±6,86		9,39±3,91		20,84±20,19		8,22±13,03	
Total	175	26,67±7,43		9,45±3,85		21,27±17,37		7,29±11,19	

Table 3. Comparison of thyroid hormones

		TSH		FT4		FT3	
	N	Mean± Std. Deviation	P	Mean± Std. Deviation	P	Mean± Std. Deviation	P
Opiate	35	1,087±97	0,023*	0,99±0,15	0,467	3,52±0,69	0,756
Non Opiate	30	1,76±1,17		1,02±0,25		3,35±0,44	
Multiple	110	1,05±1,03		1,83±8,94		3,52±0,69	
Total	175	1,13±1,05		1,57±7,41		3,51±0,67	

There was a significant difference between the opiate use group and the multiple substance use group among TSH values (p=0.02).

Discussion

Among the 160 patients who were hospitalized due to substance use disorder between 2015 and 2017, 15 (9.4%) patients had diagnosed non-opiates use disorder, 35 (21.8%) opiates and 110 (68.8%) multiple substance use disorder. In the studies, substance preference data differ. The difference may be affected by factors such as city size, level of economic development and income and education levels of individuals [10].

There was no statistically significant difference between the groups classified according to the type of substance used according to intravenous use. Of the 145 patients with opiate use, 27 had intravenous use. It is thought that those who do not have intravenous use in patients with opiate dependency are more likely to seek treatment and this may be due to the fact that this way of use is not widespread in our country. It is known that there are various ways of opiate use in the world. In the studies performed in the United States, the most frequent way to use is intravenous. In our country, this type of use has increased in recent years [11]. Although there are studies showing the effects of opiate use on the hypothalamic-pituitary axis, the data are limited and do not show consistency among themselves. In the literature, it has been shown that morphine administration leads to a decrease in TSH level and thyroid weight in observation studies [12]. In another study, patients with opiate use disorder were compared with healthy controls and TSH levels were found to be lower [13]. In our study, it was observed that TSH levels were low in opiates and in multiple substance users. In a study by Zang et al., heroin addicts and healthy control group were compared; TSH levels were repeated in the study group at the beginning of the treatment and at certain periods of time. Initially, TSH levels were low, but these values increased in remission. Free T3 and free T4 fluctuations were observed during the 3-month follow-up period [14]. In our study, TSH values were significantly lower in the opiate group than normal values (normal range between 0.5-4.5 uU/ml). This result suggests that the effect of TSH on opiate users will not lead to clinically significant results.

In some studies, it is claimed that opiates cause changes in the thyroid gland due to their effects on free T3 and free T4 levels. In these studies, there was no statistically significant difference in the TSH levels in opiate users, whereas free T3 and free T4 levels were found to be variable [15-17]. In our study, when the free T3 and free T4 levels were compared, there was no significant difference in opiate users compared to the other groups (p=0.75, p=0.46). This suggests that the effect of opiates on the thyroid gland is not limited to thyroid hormones.

A study indicates that opiates do not affect thyroid function through pituitary or peripheral hormones, suppressing the release of TRH from the hypothalamus, thus reducing TSH secretion [18]. TRH plays an important role in the release of TSH from the pituitary gland and the opiates used are likely to affect this axis. The findings in our study may support this situation, but different studies are needed to reinforce this hypothesis as the content of our study does not directly address TRH changes. When we look at non-opiate substances, there are limited data showing that psychoactive substances also affect thyroid function.

In a study on methamphetamine use, TSH and T3 levels decreased and T4 levels increased [19]. In a case report, sudden onset hyperthyroidism (thyroid storm) was observed after the first methamphetamine use, and TSH levels were significantly lower [20]. In our study, the direct psychostimulant effect was not investigated and it was determined that opiates were more affected the TSH level when compared with patients with psychostimulant use and thyroid dysfunction in patients with opiate use. The duration of substance use was significantly longer and the serum TSH level was significantly lower. Longer substance use is likely to affect serum TSH levels more.

Limitations

Our study has some limitations, mainly due to its retrospective and naturalistic design.

Changes in the thyroid function tests during the period in which the groups used the substance could not be evaluated. In addition, thyroid parenchyma and thyroid autoantibody levels are not known. Another limitation is that there are significant differences in the duration of substance use.

Conclusion

TSH levels were lower in the two groups with the use of opiates. These data indicate that opiate use has an effect on the thyroid gland and that opiate use may affect thyroid function, especially through TSH.

However, substances such as methamphetamine, which are psychostimulant, may also impair thyroid functions, but a direct result could not be reached in the study. There is a need for studies in which larger samples, thyroid autoantibodies and other factors affecting thyroid functions such as TRH are examined and repeated tests are performed in follow-up. Such studies will contribute to more objective conclusions and a certain degree of consensus.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest

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